Original Research Article

A study to assess the effect of intravenous dexmedetomidine oncis-atracurium induced neuromuscular blockade -A prospective double blind randomized controlled study

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Abstract

Introduction: Ideal neuromuscular blocking agent should act through the mechanism of nondepolarizing agent, have rapid onset of action, be highly potent, have rapid recovery and completely reversible by cholinesterase inhibitors, should not release histamine, should have good hemodynamic stability, with pharmacologically inactive metabolites and effects should be non-cumulative. **Materials and Methods:** Sixty patients of ASA physical status 1 &2 aged 18-60 years of both gender undergoing general anaesthesia for surgery lasting less than 2 hours were randomly allocated into two groups (n=30), group D received dexmedetomidine 1µg/kg iv diluted to 10 ml infusion and group C received equal volume of normal saline infusion ten mins prior to propofol induction and both groups were relaxed with Inj cisatracurium 0.15mg/kg. Neuromuscular transmission was assessed by NMT (Avance GE). Time of onset of neuromuscular blockade i.e time to achieve TOF count 0, duration of neuromuscular blockade (till TOF ratio of 0.6 / TOF count of 2) and recovery time that is time from administration of reversal at TOF ratio of ≥0.65/TOF 3 till extubation was noted. Infusion of normal saline or Inj dexmedetomidine 0.5µg/kg was started at the same rate via infusion pump during maintenance. Anaesthesia was maintained with oxygen, nitrous, isoflurane and Inj cisatracurium 0.03 mg/kg iv boluses for muscle relaxation. **Results:** In the control group mean duration was 46.80 ± 6.74 min and recovery time was 15.93 ± 2.79 min and in dexmedetomidine group mean duration was 60.40 ± 9.36 min and recovery time was 19.60 ± 2.82 min, which is statistically significant however there was no significant difference in mean time taken for onset of neuromuscular blockade. **Conclusion:** Intravenous dexmedetomidine prior to induction and during maintenance prolongs duration and recovery of cisatracurium induced neuromuscular blockade.

Key Words: dexmedetomidine; cisatracurium; neuromuscular blockade;TOF

Introduction

Ideal neuromuscular blocking agent should act through the mechanism of nondepolarizing agent, have rapid onset of action, be highly potent, have rapid recovery and completely reversible by cholinesterase inhibitors, should not release histamine, should have good hemodynamic stability, with pharmacologically inactive metabolites and effects should be non-cumulative.

Cisatracurium, an isomer of atracurium is a benzylisoquinolinium non-depolarising muscle relaxant, comprises approximately 15% of atracurium by weight with more than 50% of neuromuscular blocking activity and like atracurium is eliminated by Hoffmann elimination[1]. It is approximately four times as potent as atracurium, and in contrast to it, cis-atracurium is devoid of histamine releasing properties and has greater cardiovascular stability without cerebral and cardiovascular hemodynamic side effects. But the only disadvantage being time of onset of cis-atracurium is longer than that of atracurium[2].

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During the induction of anaesthesia, patients may be at risk of aspiration while awaiting full muscle relaxation. Thus, if the time for the onset of muscle relaxation is decreased, risk of aspiration would be reduced[3]. Dexmedetomidine is a highly selective and potent α2 adrenergic agonist, more selective for α2 than α1 Dexmedetomidine although does not have a direct effect on neuromuscular receptors has been reported to increase plasma rocuronium concentration, decreases T1 response(train of four) and increases systolic blood pressure and thus was concluded that dexmedetomidine induced vasoconstriction may alter the pharmacokinetics of rocuronium[4,5].

Hence this study is undertaken to assess the effectiveness of dexmedetomidine on the onset, duration of neuromuscular blockade and its effect on recovery with cisatracurium.

Aims and objectives

1. To assess the effects of dexmedetomidine on onset, duration and recovery of cisatracurium induced neuromuscular blockade.
2. To assess the safety profile of study drugs in patients undergoing surgery under general anaesthesia.

Materials and methods

A Prospective randomized controlled, double blind study was conducted in sixty patients undergoing elective surgery under general anaesthesia in hospitals attached to Bangalore medical college and research institute, Bangalore. The study was conducted over period of two years from November 2017-May 2019.

Inclusion criteria

1) Patient who are willing to give informed consent.
2) Patients of age 18-60 years of either sex.

3) ASA grade I and II.
4) Patients scheduled for elective surgery lasting for 90-120 mins under general anaesthesia.

Exclusion criteria

1) Patients who are not willing to give informed consent.
2) ASA grade III and above.
3) Age <18 and >60 years.
4) Use of medications that could affect the neuromuscular blockade such as calcium channel inhibitors, anticonvulsants and lithium carbonate.
5) Patients with hemodynamic instability.
6) Presence of systemic disorders involving respiratory, cardiac, renal or hepatic system.
7) Patients with neuromuscular and musculoskeletal disorders.
8) Patients with anticipated difficult airway.

After obtaining ethical committee clearance and informed written consent from patients, they were randomized using numbers generated from www.randomizer.org website and assigned to one of the two groups:

Group D: Dexmedetomidine group, 30 patients.
Group C: Control group, 30 patients

A routine pre-anaesthetic examination was conducted on the evening before surgery

• History and general condition of the patient.
• Airway assessment by Mallampati grading.
• Nutritional status, height and weight of the patient.
• A detailed examination of the cardiovascular system, Respiratory system and Central
nervous system.

The following investigations were done in all patients

• Haemoglobin
• Standard 12-lead electrocardiogram
• Random blood sugar
• Blood urea and Serum creatinine

Other investigation if indicated

The patients were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150mg orally at bed time on the previous night before surgery. They were kept nil orally from 10 pm onwards on the previous night.

A proforma was used to collect the data which included patient's particulars, indication for surgery, the anaesthetic details, intraoperative monitoring

The study drug was prepared by anesthesiologist not involved in the study

Group C: Received normal saline 10 ml IV over 10 min prior to induction of anaesthesia, followed by infusion of normal saline till end of the surgery at the same rate.

Group D: Received dexmedetomidine 1µg/kg IV diluted to 10 ml with normal saline over 10 min prior to induction of anaesthesia, followed by infusion of dexmedetomidine 0.5µg/kg for maintenance till the end of surgery.

Anaesthetic procedure

Intravenous access was established and an IV infusion of Ringer lactate was started

Monitoring included electrocardiography (ECG), plethysmography (SpO2), non-invasive blood pressure (NIBP), end tidal carbon di oxide (EtCO2), train of four (TOF).

Neuromuscular transmission was assessed by kinemyography of the adductor pollicis using mechanosensors with TOF using neurotransmission module and was displayed on anaesthesia monitoring system (S/5 TM Datex Ohmeda Avance GE). The ulnar nerve was used for stimulation response. Surface electrodes were placed on cleaned skin over the ulnar nerve on the volar aspect of wrist.

All the patients were premedicated with Inj glycopyrrolate 0.005mg/kg IV, Inj midazolam 0.03mg/kg IV and Inj fentanyl 2µg/kg IV before induction, Patients in group C received 10 ml of normal saline and group D received dexmedetomidine 1µg/kg diluted to 10ml with normal saline via infusion pump as a loading dose 10 minutes prior to induction.

Side effects of dexmedetomidine like bradycardia and hypotension were looked for. Bradycardia is defined as heart rate <50/min and will be treated with Inj atropine 0.6 mg IV. Hypotension is defined as drop in Systolic blood pressure to > 20% of baseline and was treated with rapid bolus of IV fluids and Inj ephedrine 6mg bolus.

After preoxygenation for 3 minutes with 100% oxygen, patients in each group were induced by Inj propofol 2mg/kg and dose required for loss of eyelash reflex was noted and was followed by Inj cisatracurium 0.15mg/kg. Time of Onset of neuromuscular blockade was noted, ie time taken to achieve TOF count 0, laryngoscopy and intubation was done with appropriate sized cuffed endotracheal tube. Intubation difficulty scale and Cormack lehane grading was assessed. Infusion of normal saline or Inj dexmedetomidine 0.5µg/kg was started via infusion pump at the same rate. Anaesthesia was maintained with oxygen 33%, nitrous Oxide 66% and isoflurane with MAC of 1-2%, Inj cisatracurium 0.03 mg/kg was given for maintenance of muscle paralysis**.** Duration of neuromuscular blockade (TOF 0 till TOF ratio of 0.6 i.e TOF count of 2) was noted. Infusion of normal saline/dexmedetomidine was stopped at the start of closure. Isoflurane was switched off at the last suture. At the end of surgery patient was reversed with Inj glycopyrrolate 0.01mg/kg IV and Inj neostigmine 0.05mg/kg IV and extubated at the TOF ratio of 0.9 i.e at TOF count of 4 and recovery time, i.e time from giving reversal at TOF ratio of ≥0.65 (TOF 3) till extubation was noted.

Parameters measured

1) HR, oxygen saturation, SBP, DBP, MAP, EtCO2 before administering the study drug, after giving the study drug, after induction, before intubation, immediately after intubation, at 2 minutes, 4 minutes, 6 minutes, 8 minutes and 10 minutes and every 10 minutes till the end of surgery and TOF count was noted. Post operatively patients were monitored for side effects of dexmedetomidine from the time of study drug administration till 24hours. Specific side effects looked for are: Pain on injection of Propofol, Bradycardia, hypotension, bronchospasm, flushing, pruritis, arrhythmias, nausea, vomiting.

Results

Table 1: Age distribution comparison between two groups

		Age (yrs)		P Value
		Mean	SD	
Group	Control Group	44.27	11.14	0.088
	Dexmedetomidine Group	49.40	11.75	

In the Dexmedetomidine Group mean age of subjects was 49.40 ± 11.75 years. In Control Group mean age of subjects was 44.27 ± 11.14 years. There was no significantdifference in mean age between two groups

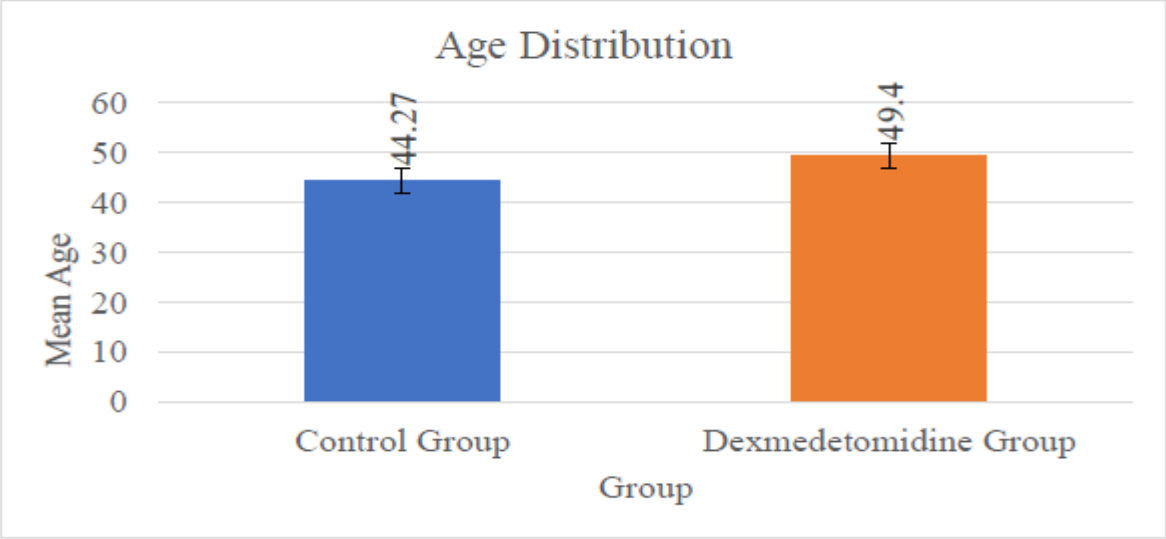

Fig 1: Bar Diagram for mean Age distribution comparison between two groups.

Table 2: Sex distribution comparison between two groups

		Sex			
		Female		Male	
		Count	%	Count	%
Group	Control Group	14	46.7%	16	53.3%
	Dexmedetomidine Group	10	33.3%	20	66.7%

χ 2 =1.111, df =1, p =0.292

In Dexmedetomidine Group, 33.3% were females and 66.7% were males. In ControlGroup, 46.7% were females and 53.3% were males.

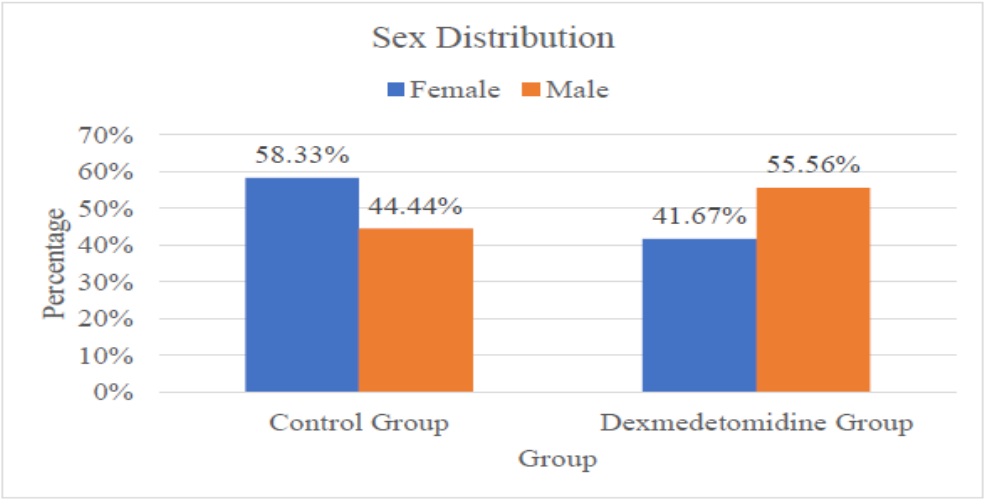

Fig 2: Bar Diagram for Sex distribution comparison between two groups.

Table 3: Weight Distribution between two groups

	Group				P Value
	GROUP C		Group D		
	Mean	SD	Mean	SD	
Weight	59.57	9.41	59.97	7.65	0.857

Mean weight in Group C was 59.57 ± 9.41 Kgs and in Group Dwas 59.97 ± 7.65 Kg. There was no significant difference in mean weight between two groups.

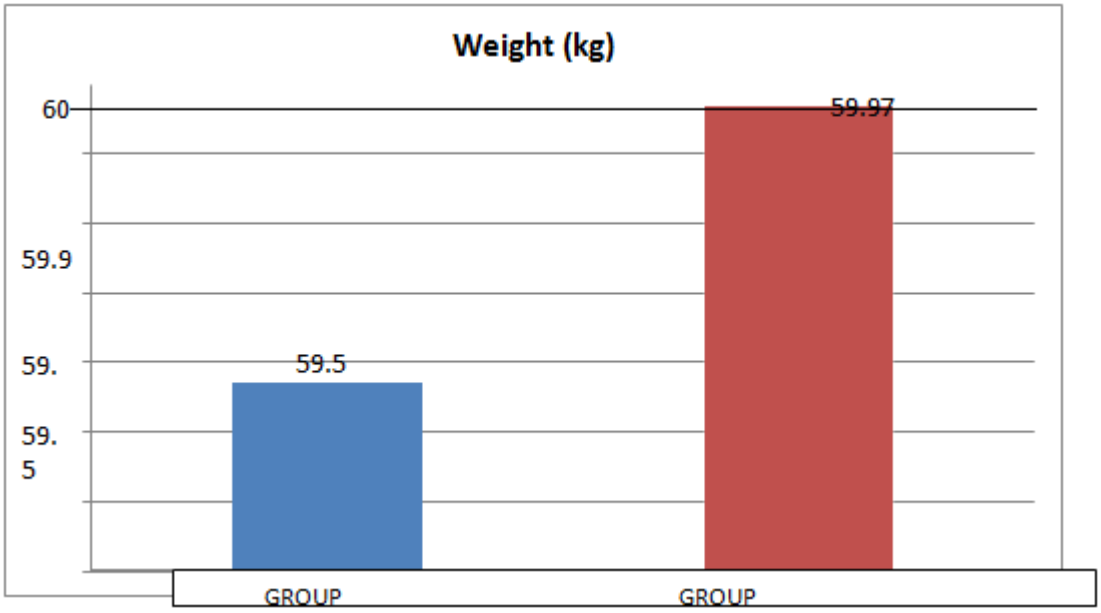

Fig 3: Bar diagram showing Weight Distribution between two groups

Table 4: Intubation difficulty score distribution comparison between two groups.

		Group			
		Control Group		Dexmedetomidine Group	
		Count	%	Count	%
Intubation DifficultyScore	0	4	13.33%	8	26.67%
	1	10	33.33%	16	53.33%
	2	10	33.33%	6	20.00%
	3	4	13.33%	0	0.00%
	4	2	6.67%	0	0.00%

$\chi 2 = 9.718$, df =4, p =0.045*

In the Dexmedetomidine Group, majority (53.33%) had Intubation Difficulty Score of 1, in Control Group, majority of subjects (33.33%) had intubation difficulty score of 1 and 2. There was significant difference in Intubation Difficulty Score between Control and Dexmedetomidine Group.

Table 5: Cormack Lehane grading distribution comparison between two groups

		Group			
		Control Group		Dexmedetomidine Group	
		Count	%	Count	%
Cormack LehaneGrading	1	12	40.00%	16	53.33%
	2	16	53.33%	12	40.00%
	3	2	6.67%	2	6.67%

$\chi 2 = 1.143$, df =2, p =0.565

In the Dexmedetomidine Group, majority (53.33%) had Cormack Lehane Grade 1, in Control Group, majority of subjects (53.33%) had Cormack Lehane Grade 2. Howeverthere was no significant difference in Cormack Lehane Grade between Control and Dexmedetomidine Group.

Table 6: Dose of Propofol for loss of eyelash reflex mean comparison betweentwo groups

		Dose Of Propofol For Loss Of Eyelash Reflex		P Value
		Mean	SD	
Group	Control Group	108.67	14.32	< 0.001*
	DexmedetomidineGroup	88.00	9.97	

In Dexmedetomidine Group mean dose of Propofol was 88.00 ± 9.97 mg and in Controlgroup mean dose of Propofol was 108.67 ± 14.32 mg. There was significant differencein mean dose of propofol for loss of eyelash reflex between two groups.

Table 7: Onset time, Duration and Recovery Time Mean comparison betweentwo groups

	Group				P Value
	Control Group		Dexmedetomidine Group		
	Mean	SD	Mean	SD	
Time Taken (Min) For Onset TOF-0	4.00	0.91	4.13	0.73	0.534
Duration (Min) TOF -2	46.80	6.74	60.40	9.36	< 0.001*
Recovery time(Min)	15.93	2.79	19.60	2.82	< 0.001*

In the Control group mean duration (TOF count of 2) was 46.80 ± 6.74 min and in Dexmedetomidine group was 60.40 ± 9.36 min. There was significant difference in mean duration between two groups.
In the control group mean recovery time (Min) was 15.93 ± 2.79 min and in dexmedetomidine group was 19.60 ± 2.82 min. There was significant difference in mean recovery time between two groups.
In the study there was no significant difference in the mean time taken for onset of neuromuscular blockade.

Table 8: Heart rate comparison between two groups at different time intervals

HR	Group						P Valueb/w 2 groups
	Control Group			Dexmedetomidine Group			
	Mean	SD	P valuewith in group	Mean	SD	P valuewith ingroup	
Baseline	82.13	10.12		82.53	9.31		0.874
After Study Drug Administration	81.13	10.46	0.097	76.00	7.71	<0.001*	0.035*
After Induction	77.47	10.38	<0.001*	74.00	8.34	<0.001*	0.159
After Intubation	85.73	11.93	<0.001*	75.27	9.34	<0.001*	< 0.001*
2 Min	85.40	10.66	0.003*	73.73	9.04	<0.001*	< 0.001*
4 Min	81.93	9.82	0.866	72.93	8.73	<0.001*	< 0.001*
6 Min	80.00	9.83	0.124	72.47	8.44	<0.001*	0.002*
8 Min	77.47	9.87	0.001*	71.93	8.21	<0.001*	0.022*
10 Min	77.20	7.70	<0.001*	72.13	9.45	<0.001*	0.027*
20 Min	78.13	7.22	0.011*	72.13	8.74	<0.001*	0.005*
30 Min	77.47	8.76	0.001*	72.60	8.82	<0.001*	0.036*
45 Min	77.67	9.25	<0.001*	71.83	9.01	<0.001*	0.016*
60 Min	79.71	9.73	0.036*	71.07	8.89	<0.001*	0.001*
75 Min	83.71	5.25	0.088	73.68	8.60	<0.001*	0.001*
90 Min	85.00	7.63	0.178	79.00	4.41	<0.001*	0.075
105 Min	78.00	.00	-	73.50	1.73	0.003*	0.026*
120 Min	73.00	.00	-	75.00	1.15	0.002*	0.082
Post Op Immediate	86.07	9.40	0.015*	73.73	6.43	<0.001*	< 0.001*
Post Op 15 Min	82.67	9.54	0.778	71.27	5.15	<0.001*	< 0.001*
Post Op 30 Min	79.73	9.33	0.154	69.73	3.85	<0.001*	< 0.001*
Post Op 60 Min	77.00	8.40	0.001*	70.13	3.66	<0.001*	< 0.001*
Post Op 2 Hr	78.27	8.59	0.018*	69.73	3.63	<0.001*	< 0.001*
Post Op 4 Hr	78.47	9.88	0.024*	70.40	3.82	<0.001*	< 0.001*
Post Op 6 Hr	78.80	8.30	0.086	72.00	4.88	<0.001*	< 0.001*
Post Op 8 Hr	78.93	7.82	0.118	72.20	5.49	<0.001*	< 0.001*
Post Op 12 Hr	79.07	6.71	0.029*	72.80	5.74	<0.001*	< 0.001*
Post Op 16 Hr	78.73	8.28	0.047*	74.20	4.87	<0.001*	0.012*
Post Op 20 Hr	78.47	6.98	0.042*	75.67	5.20	0.001*	0.083
Post Op 24 Hr	78.67	7.64	0.047*	77.07	5.49	0.008*	0.355

With in the control group, there was significant decrease in HR after induction, after intubation, at 2 min, 8 min, 10 min to 60 min, post op immediate, post op 60 min to post op 4 hr and from post op 12 hrs to post op 24 hr compared to baseline HR.
With in the Dexmedetomidine Group, there was very significant decrease in Heart rate from After Study Drug Administration to post op 24 hr compared to baseline. Hence the decrease in HR was high in Dexmedetomidine Group compared to Control group.
In the study there was significant difference in mean Heart rate between two groups at all the intervals of follow up except at Baseline, After Induction, 90 min after intubation, 120 min after intubation, Post Op 20 Hr and Post Op 24 Hr.

Table 9: SBP comparison between two groups at different time intervals

SBP	Group						P Valueb/w 2 groups
	Control Group			Dexmedetomidine Group			
	Mean	SD	P valuewith ingroup	Mean	SD	P value within group	
Baseline	124.27	10.55		125.93	9.41		0.521
After Study DrugAdministration	122.93	9.91	0.081	120.07	12.12	<0.001*	0.320
After Induction	103.87	15.55	<0.001*	106.13	12.24	<0.001*	0.533
After Intubation	125.60	12.28	0.513	110.53	12.46	<0.001*	<0.001*
2 Min	124.33	11.04	0.969	112.07	10.79	<0.001*	<0.001*
4 Min	124.13	9.84	0.926	113.53	8.44	<0.001*	<0.001*
6 Min	120.53	10.17	0.027*	114.93	8.10	<0.001*	0.022*
8 Min	120.53	9.55	0.002*	115.27	8.24	<0.001*	0.026*
10 Min	119.20	11.86	<0.001*	115.27	8.00	<0.001*	0.137
20 Min	120.73	10.92	0.004*	114.80	8.06	<0.001*	0.020*
30 Min	119.67	9.80	<0.001*	116.00	7.64	<0.001*	0.111

45 Min	118.93	10.42	<0.001*	116.20	7.62	<0.001*	0.251
60 Min	120.71	9.06	0.012*	116.10	6.64	<0.001*	0.030*
75 Min	123.29	4.12	0.049*	114.32	6.73	<0.001*	<0.001*
90 Min	128.00	2.14	0.039*	114.00	6.41	<0.001*	< 0.001*
105 Min	128.00	.00	-	105.00	8.08	<0.001*	0.019*
120 Min	130.00	.00	-	105.00	5.77	<0.001*	0.004*
Post Op Immediate	130.60	10.13	<0.001*	121.80	6.24	0.012*	<0.001*
Post Op 15 Min	126.13	7.95	0.114	118.53	6.83	0.001*	<0.001*
Post Op 30 Min	124.07	9.35	0.853	119.00	5.60	0.002*	0.014*
Post Op 60 Min	119.47	10.67	<0.001*	118.93	4.63	0.001*	0.803
Post Op 2 Hr	120.53	10.20	0.008*	120.20	4.67	0.003*	0.871
Post Op 4 Hr	121.00	8.62	0.011*	120.07	3.99	0.005*	0.593
Post Op 6 Hr	119.07	9.12	0.001*	120.80	5.45	0.020*	0.375
Post Op 8 Hr	119.27	10.77	<0.001*	123.27	4.79	0.126	0.068
Post Op 12 Hr	122.27	8.82	0.106	123.33	5.11	0.131	0.569
Post Op 16 Hr	121.33	8.46	0.068	123.73	6.47	0.185	0.222
Post Op 20 Hr	120.93	10.04	0.044*	124.13	6.15	0.253	0.142
Post Op 24 Hr	121.47	9.64	0.085	125.20	6.19	0.647	0.080

With in the control group, there was significant decrease in SBP after induction, from 6 min to 60 min, at post op immediate period, post op 60 min to post op 8 hr and at postop 20 hr compared to Baseline.

With in the Dexmedetomidine Group, there was very significant decrease in SBP from After Study Drug Administration to post op 6 hr compared to baseline. Hence the decrease in SBP was high in Dexmedetomidine Group compared to Control group.

In the study there was significant difference in mean SBP between two groups from After intubation to 8 min, at 20 min, from 60 min to Post op 30 min. At these intervalsmean SBP was significantly higher in Control group than in Dexmedetomidine Group.

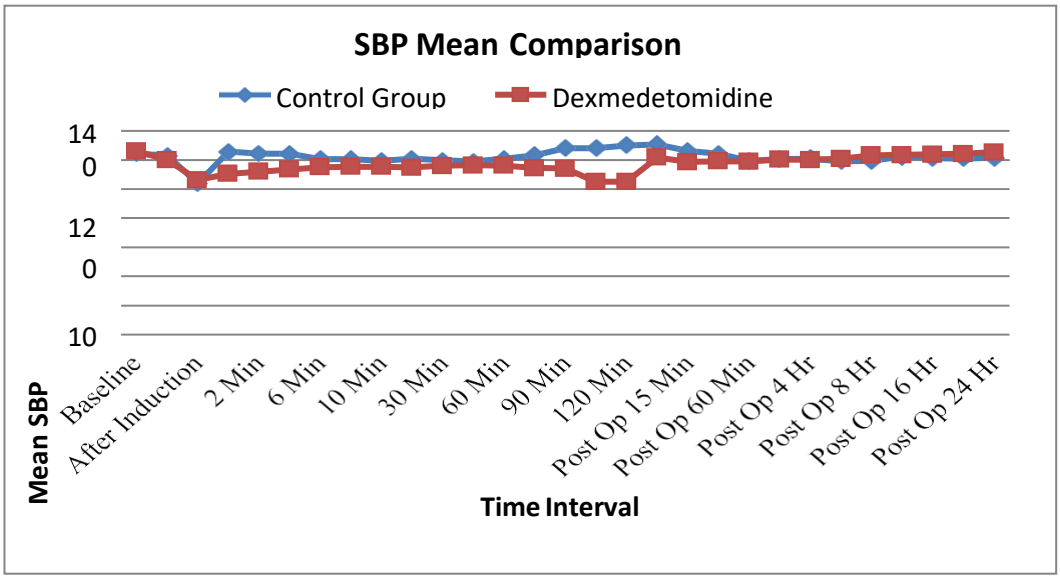

Figure 4: Line Diagram for SBP comparison between two groups at differenttime interval.

Table 10: DBP comparison between two groups at different time intervals

DBP	Group						P Valueb/w 2 groups
	ControlGroup		P valuewith in group	xmedetomidineGroup		P valuewithin group	
	Mean	SD		Mean	SD		
Baseline	76.40	10.69		77.87	6.58		0.525
After Study Drug Administration	75.80	11.00	0.258	72.53	6.19	<0.001*	0.162
After Induction	68.20	10.73	<0.001*	68.27	7.16	<0.001*	0.978
After Intubation	72.67	9.65	<0.001*	68.93	6.25	<0.001*	0.081
2 Min	73.73	8.28	0.015*	69.07	6.72	<0.001*	0.020*
4 Min	73.13	7.92	0.004*	68.93	6.03	<0.001*	0.024*
6 Min	70.73	6.84	<0.001*	68.67	6.79	<0.001*	0.245
8 Min	70.07	5.96	<0.001*	68.33	5.11	<0.001*	0.232
10 Min	71.40	6.23	<0.001*	68.00	5.04	<0.001*	0.024*
20 Min	71.87	7.36	0.002*	68.27	5.75	<0.001*	0.039*
30 Min	71.80	8.91	<0.001*	67.80	4.49	<0.001*	0.032*

45 Min	73.07	9.12	0.003*	68.63	5.59	<0.001*	0.027*
60 Min	73.07	8.40	0.033*	68.17	5.95	<0.001*	0.013*
75 Min	75.29	6.50	0.035*	69.73	5.21	<0.001*	0.008*
90 Min	78.00	3.38	0.004*	72.00	6.23	<0.001*	0.031*
105 Min	76.00	.00	-	69.50	2.89	0.025*	0.040*
120 Min	80.00	.00	-	71.00	3.46	0.027*	0.026*
Post Op Immediate	75.33	9.70	0.416	71.33	4.50	<0.001*	0.045*
Post Op 15 Min	73.27	9.16	0.025*	71.40	3.32	<0.001*	0.298
Post Op 30 Min	70.73	10.00	<0.001*	71.27	3.37	<0.001*	0.783
Post Op 60 Min	71.13	7.56	0.002*	71.20	3.77	<0.001*	0.966
Post Op 2 Hr	73.13	7.64	0.041*	71.87	3.73	<0.001*	0.418
Post Op 4 Hr	72.73	8.17	0.016*	73.00	4.65	<0.001*	0.877
Post Op 6 Hr	71.00	7.51	0.001*	74.40	4.77	0.016*	0.041*
Post Op 8 Hr	73.80	7.03	0.058	74.93	4.76	0.044*	0.468
Post Op 12 Hr	75.47	8.71	0.501	76.20	3.45	0.204	0.670
Post Op 16 Hr	73.93	9.57	0.142	77.67	3.52	0.879	0.050
Post Op 20 Hr	74.80	8.75	0.287	77.53	3.38	0.734	0.116
Post Op 24 Hr	73.67	9.30	0.139	79.73	4.01	0.116	0.002*

With in the control group, there was significant decrease in DBP after induction to 90 min, and from post op 15 min to post op 6 hrs compared to baseline DBP. With in the Dexmedetomidine Group, there was very significant decrease in DBP from After Study Drug Administration to post op 8 hr compared to baseline. Hence the decrease in DBP was high in Dexmedetomidine Group compared to Control group. In the study there was significant difference in mean DBP between two groups at 2 min, 4 min, 10 min to immediate Post op, at Post op 6 hr and Post Op 24 hr. At these intervalsmean DBP was significantly higher in Control group than in Dexmedetomidine Group.

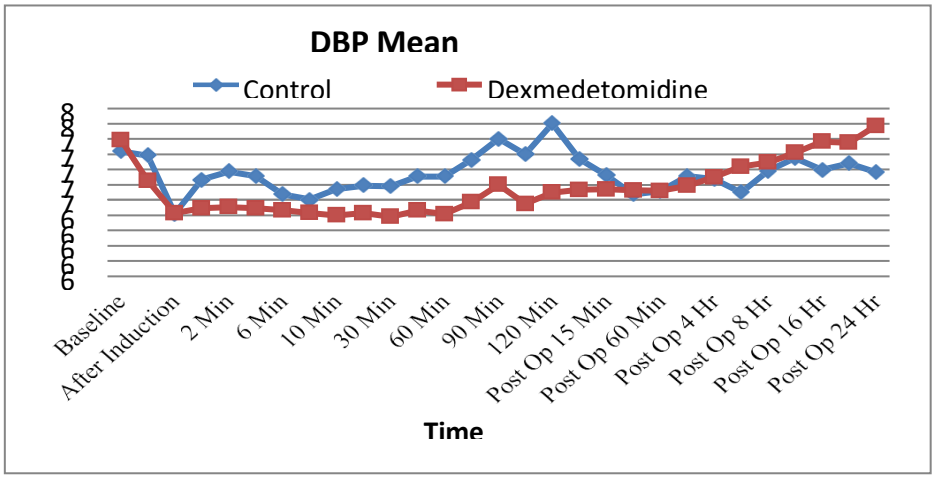

Figure 5: Line Diagram for DBP comparison between two groups at differenttime interval.

Table 11: MAP comparison between two groups at different time intervals

MAP	Group						P Valueb/w 2 groups
	Control Group			Dexmedetomidine Group			
	Mean	SD	P value with ingroup	Mean	SD	P value with ingroup	
Baseline	92.36	10.13		93.89	5.96		0.478
After Study DrugAdministration	92.36	10.13	0.006*	88.38	6.68	<0.001*	0.078
After Induction	91.51	10.22	0.004*	80.89	6.46	<0.001*	<0.001*
After Intubation	80.09	11.42	<0.001*	82.80	5.84	<0.001*	0.252
2 Min	90.60	8.08	0.075	83.40	5.94	<0.001*	< 0.001*
4 Min	90.13	7.69	0.023*	83.80	5.31	<0.001*	<0.001*
6 Min	87.33	7.17	<0.001*	84.09	5.52	<0.001*	0.054
8 Min	86.89	6.73	<0.001*	83.98	3.93	<0.001*	0.045*
10 Min	87.33	7.53	<0.001*	83.76	4.33	<0.001*	0.028*
20 Min	88.16	7.39	<0.001*	83.78	4.79	<0.001*	0.009*
30 Min	87.76	8.58	<0.001*	83.87	3.98	<0.001*	0.028*
45 Min	88.36	9.01	<0.001*	84.49	4.61	<0.001*	0.041*
60 Min	88.95	8.43	0.005*	84.14	4.43	<0.001*	0.008*
75 Min	91.29	5.53	0.006*	84.59	3.75	<0.001*	<0.001*
90 Min	94.67	2.57	<0.001*	86.00	5.09	<0.001*	0.001*

105 Min	93.33	0.00	-	81.33	0.77	0.007*	<0.001*
120 Min	96.67	0.00	-	82.33	0.38	0.003*	< 0.001*
Post Op Immediate	93.76	9.43	0.133	88.16	4.00	<0.001*	0.004*
Post Op 15 Min	90.89	8.43	0.168	87.11	3.52	<0.001*	0.027*
Post Op 30 Min	88.51	9.33	<0.001*	87.18	3.34	<0.001*	0.464
Post Op 60 Min	87.24	7.84	<0.001*	87.11	3.07	<0.001*	0.931
Post Op 2 Hr	88.93	7.86	0.005*	87.98	2.94	<0.001*	0.535
Post Op 4 Hr	88.82	7.52	0.001*	88.69	3.44	<0.001*	0.930
Post Op 6 Hr	87.02	7.54	<0.001*	89.87	4.03	0.002*	0.074
Post Op 8 Hr	88.96	8.03	0.005*	91.04	3.54	0.019*	0.198
Post Op 12 Hr	91.07	8.55	0.247	91.91	3.22	0.058	0.614
Post Op 16 Hr	89.73	8.82	0.069	93.02	3.53	0.373	0.063
Post Op 20 Hr	90.18	8.06	0.061	93.07	3.42	0.250	0.076
Post Op 24 Hr	89.60	8.60	0.057	94.89	4.04	0.218	0.003*

Discussion

Dexmedetomidine is a highly selective, non subtype-specific α2 agonist, it has anaesthesia sparing effects and it decreases heart rate blood pressure and cardiac output in a dose dependent manner. The neuromuscular effects are unknown in humans and henceforth we studied the effects of dexmedetomidine on neuromuscular block during propofol and fentanyl anaesthesia[6].

α 2 agonist decrease blood pressure by centrally mediated sympatholytic effects and by decreasing norepinephrine release via peripheral presynaptic α2 receptor stimulation. In addition α2 agonist induce peripheral vasoconstriction by directly activating vascular smooth muscle α2 receptors. The hemodynamic effects of α2 agonist therefore should be a combination of their sympatholytic and vasoconstrictive effects[7].

We conducted a study on 60 patients of ASA physical status 1 & 2, age ranging between 18 to 60 years, undergoing elective surgeries under general anaesthesia lasting not more than 120 mins who were randomly allocated into two groups of 30 each. We excluded patients with hypertension, diabetes, cardiovascular disease, renal dysfunction and pregnancy[8].

In our study, distribution of age ranged between 18-60 years with mean age of distribution in dexmedetomidine group was 49.40 ±11.75 years and in normal saline group was 44.27±11.14 years. The sex difference and the distribution of ASA class between the groups are statistically insignificant, hence demographic characteristics are comparable in both groups[9,10].

Dose of propofol required

Avneesh, Satya et al (2018) conducted study on Forty patients undergoing laparoscopic cholecystectomy were randomly allocated to receive either dexmedetomidine (Group A; n = 20) or normal saline (Group B; n = 20). In Group A, before anaesthesia induction a loading dose of dexmedetomidine (1 μg/kg) followed by infusion of (0.6 μg/kg/h) during surgery was adminstered. Anesthesia was induced with propofol, and maintenance infusion rate was adjusted to a BIS of 55–60 in both groups. Mean arterial pressure (MAP) and heart rate (HR) were recorded at baseline and at various time points from loading of drugs to just after tracheal extubation. Recovery time (time from end of all infusions to BIS = 80) and extubation time (time from end of all infusions to extubation) were noted. After intubation, MAP and HR values in Group A were significantly lower than Group B at various time points of study. To achieve similar BIS values, significantly low doses of propofol were required in Group A during induction and intraoperatively. Doses were reduced by 36% and 31%, respectively. Mean recovery time and mean extubation time in Group A were also significantly less and concluded that during propofol-based anesthesia for laparoscopic cholecystectomy, dexmedetomidine provides stable intraoperative hemodynamics and reduces propofol requirement for induction as well as maintenance, without compromising recovery profile. Our study had similar finding in Dexmedetomidine Group mean dose of Propofol was 88.00 ± 9.97 mg and in Control group mean dose of Propofol was 108.67 ± 14.32 mg. There was significant difference in mean dose of propofol for loss of eyelash reflex between two groups.

Our study also had similar results to above studies in the control Group mean duration was 46.80 ± 6.74 min and in dexmedetomidine group was 60.40 ± 9.36 min which is statistically significant.

In the control Group mean recovery time (Min) was 15.93 ± 2.79 min and in dexmedetomodine group it was 19.60 ± 2.82 min and there is significant difference in mean recovery time between two groups. However in our study there was no significant difference in mean time taken for onset of neuromuscular blockade between two groups.

In study conducted by Rashmi, Komala (2017) who included Sixty euthyroid patients, scheduled for thyroid surgeries and was randomly divided into two groups with 30 patients in each group. Group A (n = 30) received injection dexmedetomidine 0.6 μg/kg body weight and Group B (n = 30) received 10 ml of normal saline. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at regular intervals after intubation. In their study, following laryngoscopy and intubation at 1 min, the mean HR increased by 36 bpm in the Group B whereas in Group A the mean HR increased by only 4 bpm which is statistically highly significant (P = 0.000) when compared to control group (Group B). At 5th min, the increase in mean HR in the control group (Group B) sustained, and it was 23 bpm, whereas in Group A there was a decrease in HR by 3 which was statistically significant[45].

In our study within the control group, there was significant decrease in HR after induction, after intubation, at 2 min, 8 min, 10 min to 60 min, post op immediate, post op 60 min to post op 4 hr and from post op 12 hrs to post op 24 hr compared to baseline HR. Within the Dexmedetomidine Group, there was very significant decrease in Heart rate from After Study Drug Administration to post op 24 hr compared to baseline. Hence the decrease in HR was high in Dexmedetomidine Group compared to Control group. However there was no severe episodes of bradycardia requiring inj atropine was noted in our study groups

In study conducted by Rashmi, Komala (2017) noted that dexmedetomidine significantly attenuates stress response at intubation with lesser increase in HR (10% vs. 17%), SBP (6% vs. 23%), and DBP (7% vs. 20%) as compared to the control group (P < 0.05). Authors concluded that dexmedetomidine attenuates various stress responses during surgery and maintains the hemodynamic stability when used as an adjuvant in general anesthesia.

In our study there was significant difference in mean SBP between two groups from After intubation to 8 min, at 20 min, from 60 min to Post op 30 min. At these intervals mean SBP was significantly higher in Control group than in Dexmedetomidine Group. There was significant difference in mean DBP between two groups at 2 min, 4 min, 10 min to immediate Post op, at Post op 6 hr and Post Op 24 hr. At these intervals mean DBP was significantly higher in Control group than in Dexmedetomidine Group

In the study there was significant difference in mean MAP between two groups at all the intervals of follow up except at Baseline, After

Study Drug Administration, After Intubation, 6 min, post op 30 min to post op 24 hr.

Conclusion

We observed that administrating dexmedetomidine prior to induction required lesser dose of propofol at the time of induction, provided better intubating condition, yielded hemodynamic stability during laryngoscopy and prolonged the duration and recovery time of cisatracurium induced neuromuscular blockade, though there was no significant change in onset of neuromuscular blockade.

Hence in this study intravenous dexmedetomidine infusion prior to induction and during maintenance prolonged duration and recovery time of cisatracurim induced neuromuscular blockade.

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